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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/517,275	MIN ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) *1-21,23,25,26,28-46 and 49-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,24,27,47 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/09/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 22, 24, 27, 47 and 48 in the reply filed on 04/24/2007 is acknowledged. The traversal is on the ground(s) that the subject matter of the presently elected claims is not disclosed in the U.S. Patent No. 6,506,559 (the '559 Patent) because the '559 Patent discloses the treatment of cancer and cancer is not an "immune disorder" which is the subject matter of claim 22 and which is shared with claim 32. Therefore, applicant argues the subject matter of the presently elected claimed in not disclosed in the '559 Patent. This is not found persuasive because the instant specification at page 10 discloses a variety of immune disorders such as *cancer* that can be treated by modulating T cell activity (see lines 25-30). Thus, because the special technical feature is a construct comprising a siRNA that inhibits expression of an endogenous target gene, such as a cancer gene, encoding an enzyme for the treatment of cancer, an immune disorder, and is disclosed in the '559 Patent, the construct cannot be said to be a special technical feature under PCT Rule 13.2.

Further, applicant's election with traverse of a cytokine in claim 22, transplant rejection in claim 27 and siRNA in claim 48 in the reply filed 10/25/2006 is acknowledged. The traversal is on the ground(s) that there would not be a search burden to search all the endogenous genes cited in claim 22, both the constructs recited in claim 48 or each disorder recited in claim 27. With respect to the endogenous genes recited in claim 22, a search for a siRNA with homology to an enzyme would not

necessarily return siRNA with homology to a cytokine. Likewise, a search for a construct comprising a DNA/RNA hybrid would not return a search for a siRNA given that a search for a DNA sequence would not return results for a RNA sequence. Lastly, each of the immune disorders recited in claim 27 are different and would be regulated differently when treated with a siRNA. Therefore, a search and examination of all genes of claim 22, constructs of claim 48 and immune disorders of claim 27 is burdensome because the searches are not coextensive.

The requirement is still deemed proper and is therefore made FINAL.

Status of the Application

Claims 1-54 are pending. Claims 22, 24, 27, 47 and 48 are currently under examination. Claims 1-21, 23, 25-26, 28-46 and 49-54 and subject matter not elected are withdrawn as being drawn to a non-elected invention. It is noted in the remarks filed 04/24/2007, applicant states the claims of groups I and III were canceled, but as noted above, the claims have been withdrawn, as indicated in the claims filed 04/24/2007.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because the specification, on pages 27-28, recite sequences that do not have the required sequence identifier.

A complete response to this office action must correct the defects cited above regarding compliance with the sequence rules and a response to the action on the merits which follows.

The aforementioned instance of failure to comply is not intended as an exhaustive list of all such potential failures to comply in the instant application. Applicants are encouraged to thoroughly review the application to ensure that the entire application is in full compliance with all sequence rules. This requirement will not be held in abeyance.

Claim Rejections - 35 USC § 101 and 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 22, 24 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 provides for the use of a siRNA possessing specific homology to a region of a gene, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps

delimiting how this use is actually practiced. Claims 24 and 27 are rejected due to their dependence on claim 22.

Claims 22, 24 and 27 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). Claims 24 and 27 are rejected due to their dependence on claim 22.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim 47 is rejected under 35 U.S.C. 102(e) as being anticipated by Keshavjee et al. (US 2003/0180301).

The instant claim is drawn to a method for decreasing immunogenicity and rejection potential of an organ for transplantation, said method comprising perfusing into said organ at least one construct that inhibits the expression of an endogenous target gene encoding a cytokine and a pharmaceutically acceptable carrier.

Keshavjee et al. teach administration of a TGF-β cytokine antagonist to treat or prevent the loss of transplant function (see abstract). Keshavjee et al. teach TGF-β cytokine antagonist is an antisense oligonucleotide that reduces the gene transcription or translation of TGF-β (see paragraph 0041) and further teach pharmaceutical compositions comprising said antagonist and a pharmaceutically acceptable carrier (see paragraph 0029). The instant specification on page 6 lines 31-34, disclose a construct as any suitable construct that targets and silence a gene of interest. Therefore the antisense oligonucleotide taught by Keshavjee et al. meets the limitations of the claim and Keshavjee et al. anticipates claim 47.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 47-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keshavjee et al. as applied to claim 47 above, and further in view of Hammond et al. (Nature Reviews Genetics February, 2001) and Tuschl et al. (WO 02/44321).

The instant claim is drawn to a method for decreasing immunogenicity and rejection potential of an organ for transplantation, said method comprising perfusing into said organ at least one construct that inhibits the expression of an endogenous target gene encoding a cytokine wherein the construct is a siRNA.

Keshavjee et al. is relied upon as above. Keshavjee et al. do not teach inhibiting the expression the TGF-β cytokine antagonist using a siRNA.

Hammond et al. teach two methods for silencing specific genes: antisense and RNA interference. Hammond et al. teach that although antisense methods are straightforward techniques for probing gene function, the methods have suffered from "...questionable specificity and incomplete efficacy." (see page 110, column 1). Hammond et al. further teach " "...dsRNAs have been shown to inhibit gene expression in a sequence-specific manner" and further "RNAi is a potent method, requiring only a few molecules of dsRNA per cell to silence expression."

Tuschl et al. teach siRNA molecules and teach compositions comprising siRNA and an acceptable carrier that are capable of silencing gene expression (see page 9, lines 17-25). Tuschl et al. teach that siRNAs represent a new alternative to antisense or ribozyme therapeutics.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a siRNA molecule, as taught by Hammond et al. and Tuschl et al. to target a gene encoding TGF-β cytokine, as taught by Keshavjee et al.

One would have been motivated to use a siRNA targeted to a TGF-β cytokine gene and inhibit gene expression because Keshavjee et al. teach TGF-β cytokine expression leads to loss of organ transplant function in a host due to chronic rejection of the organ. One would have been motivated to use a siRNA targeted to a TGF-β cytokine gene instead of an antisense because it was well known at the time the invention was made that siRNA molecules are efficient molecules to target and decrease expression of a target gene and because Hammond et al. teach using siRNA to inhibit gene expression is more sequence specific than using antisense methodologies and RNAi using dsRNA is a more potent method requiring only a few molecules of dsRNA per cell. One would have been motivated to create such compounds with increased stability and functionality, and since siRNAs are taught by Tuschl et al. as being useful in silencing gene expression.

One would have a reasonable expectation of success given that Tuschl et al. teach how to make and use virtually any siRNA to any gene provided the target

sequence is known and teach that methods of RNA synthesis are known in the art, as evidenced by the examples provided therein.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has

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